Fetal tachycardia: Is digitalis still the first-line therapy?

A.P. Athanassiadis[1], *M.D., Ph.D.*; **C. Dadamogias**[1], *M.D.*; **D. Netskos**[2], *M.D.*; **G. Avramidis**[3], *M.D.*; **M. Zafrakas**[1], *M.D.*; **T. Mikos**[1], *M.D.*; **A. Apostolidis**[1], *M.D.*; **E. Asimakopoulos**[1], *M.D., Ph.D.*; **J. Bontis**[1], *Prof.*

[1]*1st Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Hippokrateion General Hospital;* [2]*Department of Neonatology, Hippokrateion General Hospital;* [3]*2nd Propedeutical Department of Internal Medicine, Aristotle University of Thessaloniki, Hippokrateion General Hospital, Thessaloniki (Greece)*

Summary

Medical treatment of fetal tachycardias has substantially improved neonatal outcome over the past years. Digitalis has been often used as first-line therapy in these cases, and more recently the use of several newer agents have been reported. We present four cases of fetal tachycardia with a favorable neonatal outcome after successful treatment with digitalis. Rapid transplacental digitalization appears to be an effective and reliable treatment option for fetal tachycardia, particularly in non-hydropic fetuses. In hydropic fetuses, however, digitalis alone appears to be less effective and administration of a second drug is usually needed.

Key words: Fetal tachycardia; Digitalis; Digoxin.

Introduction

Fetal tachycardia is a rare pregnancy complication usually of unknown etiology. It can be easily recognized with fetal heart auscultation during routine prenatal visits. In most cases it has a short duration and is of no clinical significance. Tachycardia is only rarely sustained and can be detrimental to the fetus. Due to the rarity of this condition, no general treatment guidelines exist. We present four cases of fetal tachycardia treated in our hospital between 1994 and 2002. In all cases, maternal history was unremarkable, there were no maternal symptoms, and fetal biometry was appropriate for gestational age when tachycardia was diagnosed. Intravenous digoxin was the first-line therapy in all cases; after initiation of treatment all mothers were monitored with electrocardiogram every eight hours, and there were no maternal or fetal side-effects noted.

Case Report

Case 1: A 28-year-old nulliparous woman was referred at 27 weeks' gestation due to fetal cardiac arrhythmia. Laboratory tests were normal, including testing for anti-Ro and anti-La autoantibodies. On ultrasound the fetal heart rate (FHR) was 300 bpm and there were no signs of hydrops (Figure 1). Digoxin therapy was decided on (loading dose 1 mg IV in four doses on the first day, followed by 0.25 mg/day orally). Within 24 hours, the FHR was 130 bpm. The woman was discharged with the same oral dose of digoxin and ultrasound re-examination at weekly intervals was recommended. Tachycardia recurred at 33 weeks. A cesarean section due to fetal distress was then performed and a live, male infant, weighing 2,100 g was born. Postnatally a bicuspid aortic valve was diagnosed. The child is now two years old, with normal growth and development, under constant digoxin treatment, with no signs of recurrence.

Case 2: A 30-year-old nulliparous woman was referred at 31 weeks' gestation after detection of fetal tachyarrhythmia during routine examination. Diagnosis of fetal supraventricular tachycardia was set on ultrasound (average FHR 240 bpm); there were no signs of hydrops. The glucose tolerance test was abnormal, but diet alone proved to be sufficient therapy. Rapid transplacental digitalization followed (loading dose 1.25 mg in five doses on the first day, followed by 0.25 mg/day orally), leading to normal FHR within 24 hours. The digoxin dose was temporarily reduced to 0.25 my orally/day, but tachycardia recurred making an additional dose of 0.25 mg IV digoxin/day necessary for the next three days. The woman was discharged with the recommendation to take 0.25 mg digoxin/day, orally. After vaginal delivery at term of a live female infant, weighing 2,950 g, tachycardia apparently resolved spontaneously. Pediatric evaluation showed that no cardiac anomalies were present. The child is now one year old, in good health, with a stable heart rate, and no drug treatment is needed.

Case 3: A 30-year-old nulliparous woman was referred at 22 weeks' gestation due to fetal tachycardia detected on routine ultrasound. Fetal supraventricular tachycardia exceeding 260 bpm and fetal hydrops (Figure 2) were diagnosed. The fetal cardiac anatomy was normal, but accurate evaluation was difficult because of tachycardia. A loading dose of 1.5 mg digoxin IV was given on the first day, followed by 0.75 mg on the second day, but with no response. On the third day, 160 mg of oral verapamil was added together with 0.50 mg digoxin. Fetal ascites was reduced 24 hours after the introduction of verapamil, but with no change in FHR. On the fourth day the FHR was normal. The final treatment regimen was: digoxin 0.25 mg/day orally and verapamil 120 mg/day orally. The woman delivered vaginally at term a healthy male infant weighing 3,440 g. Pediatric evaluation showed that no cardiac anomalies were present. The child is now five years old with normal growth and development.

Case 4: A 23-year-old nulliparous woman was referred at 27 weeks' gestation after detection of fetal tachycardia during routine fetal heart auscultation. On ultrasound an FHR of 240 bpm was detected. No sign of hydrops fetalis was found. Therapeutically rapid transplacental digitalization was performed

Revised manuscript accepted for publication June 1, 2004

Fig. 1

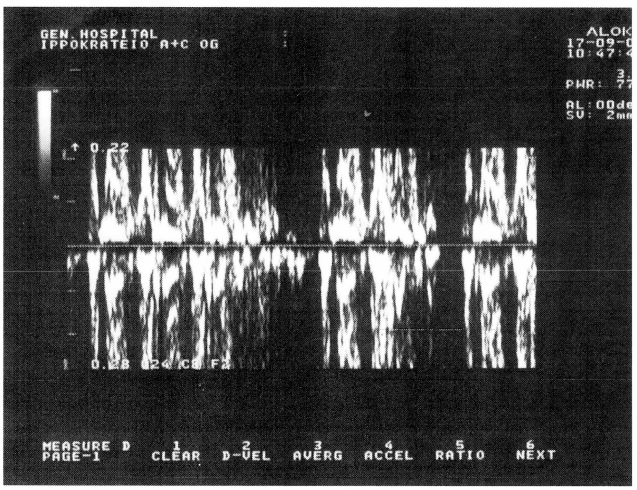

Fig. 2

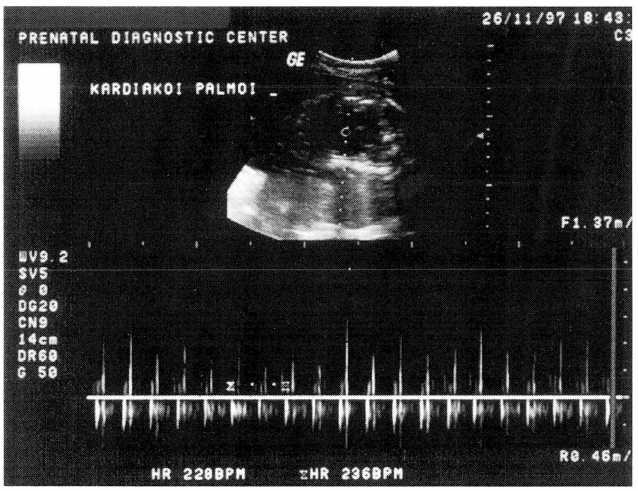

Figure 1. — Fetal heart rate (FHR) at 300 bpm (1st case, 27 weeks' gestation).
Figure 2. — Fetal supraventricular tachycardia exceeding 260 bpm (3rd case, 22 weeks' gestation)

with 1.5 mg/day digoxin leading to resolution of the tachycardia within 24 hours. The dose was then reduced to 0.25 my/day orally and tachycardia did not recur. At term, a live healthy female, weighing 3,600 g was delivered by cesarian section due to fetal distress. Postnatal evaluation did not show any cardiac anomaly. Now, two months after delivery, the child has a normal heart rate and no medications are needed.

Discussion

Fetal arrhythmias are generally divided into tachycardias (FHR > 200 bpm) and bradycardias (FHR < 100 bpm). Fetal tachycardias are classified according to their origin as premature atrial and ventricular contractions, which are benign, supraventricular tachycardias and AV block. Short-term fetal tachycardia is most often detected during routine prenatal visits. It is usually benign, and its main cause is fetal heart immaturity and instability. On the other hand, sustained tachycardia needs accurate diagnosis and proper evaluation in a specialized center with a thorough ultrasonographic examination, including fetal cardiac anatomy, M-Mode and color Doppler, and serial re-examinations.

Since fetal tachycardia is a rare condition, there are no generally accepted treatment guidelines. On the other hand there are some general principles regarding treatment options. The main objective is the birth of a live, mature baby and avoidance of heart failure. Individualization of treatment is needed, since the risks from prematurity and medication side-effects can be very dangerous. In transient tachycardia, medical treatment is not needed, since it resolves in most cases rather than deteriorating to persistent tachycardia [1]. Persistent tachycardia near term, when fetal pulmonary maturity is established, should be treated with no hesitation with delivery of the fetus: treatment of a neonate is preferable to treatment of a fetus [2]. Prior to 33 weeks, with an immature fetus, medical treatment is needed in order to avoid fetal heart failure. The above protocol helped as all the reported cases had an excellent postnatal and further developmental outcome.

There are several reports in the literature in which digoxin was used as first-line treatment of fetal tachycardia, in various IV (0.5-2 mg/day) and oral (1-2,5 mg) doses [1, 3], whith variable results. Rapid transplacental digitalization and direct intramuscular injection of digoxin to the fetus have also been reported [4, 5]. The success rate of digoxin therapy varies considerably due to fluctuation in placenta permeability, presence of hydrops and/or antomic cardiac defects [6, 7]. When digoxin fails to convert fetal tachycardia and reduce hydrops, then verapamil is useful, most often together with digoxin, in daily doses of 240 mg orallyu or 5-10 mg IV [1]. Some investigators however, have reported poor results with digoxin treatment [7].

Treatment of fetal tachycardia with other agents, including propanolol, amiodarone, sotalol, flecainide and quinidine has also been studied. Amiodarone has been used as second-line therapy in persistent tachycardia, with hydrops being the basic criterion for its administration. Despite success in controlling FHR, amiodarone has been associated with poor tolerability, and fetal hypothyroidism as a rare but severe side-effect [8, 9]. Sotatlol has been used as first-line therapy and appeared to be effective but with serious side-effects, mainly bradycardia [10, 11]. Flecainide is a very promising option in the treatment of fetal tachycardia, but it has been associated with rare but confusing side-effects: an arrhythmic state due to QT prolongation, false loss of FHR-variability and fetal hyperbilirubinemia. Thus controversy exists as to whether it should be used as first- or second-line therapy [12-15].

Our therapeutic approach in all cases was rapid transplacental digitalization with loading doses of 1-1.5 mg/day intravenously. Only in one case, where ascites was present, we had to add oral verapamil (160 mg/d)

with very good results. It has been previously reported that digoxin alone is insufficient when ascites is present; with loating IV doses lower that those given in our cases, good response to therapy has been achieved in 80-85% of non-hydropic and 60-65% of fetuses when ascites was present [1]. Postnatally, medical treatment is necessary in 80% of hydropic and 50% of non-hydropic fetuses [16]. A point of special interest is the time needed to achieve conversion of the FHR to normal levels. In most reports, digoxin was given orally and the mean time needed to convert the FHR was four to seven days. We preferred rapid transplacental digitalization and the FHR converted to normal within 24 hours. Considering the side-effects of other drugs, rapid transplacental digitalization seems to be effective, safe, and suitable as first-line therapy for fetal tachycardias, especially in non-hydropic fetuses.

References

[1] Simpson J.M., Milburn A., Yates R.W., Maxwell D.J., Sharland G.K.: "Outcome of intermittent tachyarrhythmias in the fetus". *Pediatr. Cardiol.*, 1997, *18*, 78.

[2] Simpson J.M., Sharland G.K.: "Fetal tachycardias: Management and outcome of 127 consecutive cases". *Heart,* 1998, *79*, 576.

[3] Silva I.S., Nunes C., Mimoso G., Castela E., Mesquita J.: "Digoxin. The drug of choice for the in utero treatment of paroxysmal supraventricular tachycardia". *Acta Med. Port.*, 1997, *10*, 95.

[4] Parilla B.V., Strasburger J.F., Socol M.L.: "Fetal supraventricular tachycardia complicated by hydrops fetalis: a role for direct fetal intramuscular therapy". *Am. J. Perinatol.*, 1996, *13*, 483.

[5] Barnes E.J., Eben F., Patterson D.: "Direct current cardioversion during pregnancy should be performed with facilities available for fetal monitoring and emergency caesarean section". *Br. J. Obstet. Gynaecol.*, 2002, *109*, 1406.

[6] Schmolling J., Renke K., Richter O., Pfeiffer K., Schlebusch H., Holler T.: "Digoxin, flecainide, and amiodarone transfer across the placenta and the effects of an elevated umbilical venous pressure on the transfer rate". *Ther. Drug. Monit.*, 2000, *22*, 582.

[7] Ito S.: "Transplacental treatment of fetal tachycardia: implications of drug transporting proteins in placenta". *Semin. Perinatol.*, 2001, *25*, 196.

[8] Jouannic J.M., Delahaye S., Fermont L., Le Bidois J., Villain E., Dumez Y., Dommergues M.: "Fetal supraventricular tachycardia: a role for amiodarone as second-line therapy?". *Prenat. Diagn.*, 2003, *23*, 152.

[9] Schleich J.M., Du Haut B., Cilly F., Laurent M.C., Almange C.: "Early prenatal management of a fetal ventricular tachycardia treated in utero by amiodarone with long term follow-up". *Prenat. Diagn.*, 2000, *20*, 449.

[10] Oudijk M.A., Michon M.M., Kleinman C.S., Kapusta L., Stoutenbeek P., Visser G.H., Meijboom E.J.: "Sotalol in the treatment of fetal dysrhythmias". *Circulation,* 2000, *101*, 2721.

[11] Sonesson S.E., Fouron J.C., Wesslen-Eriksson E., Winberg P.: "Foetal supraventricular tachycardia treated with sotalol". *Acta Paediatr.*, 1998, *87*, 584.

[12] Nakata M., Anno K., Matsumori L.T., Fujiwara M., Sumie M., Sase M., Kato H.: "Successful treatment of supraventricular tachycardia exhibiting hydrops fetalis with flecainide acetate. A case report". *Fetal. Diagn. Ther.*, 2003, *18*, 83.

[13] van Gelder-Hasker M.R., de Jong C.L., de Vries J.I., van Geijn H.P.: "The effect of flecainide acetate on fetal heart rate variability: a case report". *Obstet. Gynecol.*, 1995, *86*, 667.

[14] Rasheed A., Simpson J., Rosenthal E.: "Neonatal ECG changes caused by supratherapeutic flecainide following treatment for fetal supraventricular tachycardia". *Heart.,* 2003, *89*, 470.

[15] Vanderhal A.L., Cocjin J., Santulli T.V. Jr., Carlson D.E., Rosenthal P.: "Conjugated hyperbilirubinemia in a newborn infant after maternal treatment with flecainide acetate for fetal tachycardia and fetal hydrops". *J. Pediatr.*, 1995, *126*, 988.

[16] Naumburg E., Riesenfeld T., Axelsson O.: "Fetal tachycardia: intrauterine and postnatal course". *Fetal. Diagn. Ther.*, 1997, *12*, 205.

Address reprint requests to:
A.P. ATHANASSIADIS, M.D., Ph.D.
1st Department of Obstetrics and Gynecology
Hippokrateion General Hospital
Konstantinoupoleos 49
54642 Thessaloniki (Greece)